HFV-230
305

Date of Approval: FEB 3 2005

FREEDOM OF INFORMATION SUMMARY

ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-280

Euthanasia-III Solution (Euthanasia Solution)

For canine euthanasia only

Euthanasia-III Solution (Euthanasia Solution) is for use in dogs for humane, painless, and rapid euthanasia.

Sponsored by:

Med-Pharmex, Inc.

2005-200-280

FOIS 1

FREEDOM OF INFORMATION SUMMARY

1. GENERAL INFORMATION:

a. File Number:	ANADA 200-280
b. Sponsor:	Med-Pharmex, Inc. 2727 Thompson Creek Rd. Pomona, CA 91767 Drug Labeler Code: 051259-1861
c. Established Name:	Pentobarbital sodium and phenytoin sodium
d. Proprietary Name:	Euthanasia-III Solution
e. Dosage Form:	Solution
f. How Supplied:	100 mL Multiple-Dose Vial
g. How Dispensed:	Rx
h. Amount of Active Ingredients:	Each mL contains: 390 mg pentobarbital sodium (barbituric acid derivative), 50 mg phenytoin sodium.
i. Route of Administration:	Intravenous or intracardiac
j. Species/Class:	Dogs
k. Recommended Dosage:	1 mL for each 10 pounds of body weight.
l. Pharmacological Category:	Pentobarbital sodium – anesthetic Phenytoin sodium – anticonvulsant
m. Indications:	For use in dogs for humane, painless, and rapid euthanasia.
n. Pioneer Product:	BEUTHANASIA-D Special (Euthanasia Solution); pentobarbital sodium and phenytoin sodium; NADA 119-807; Schering-Plough Animal Health Corp.

2. TARGET ANIMAL SAFETY AND DRUG EFFECTIVENESS:

Under the provisions of the Federal Food, Drug, and Cosmetic Act, as amended by the Generic Animal Drug and Patent Term Restoration Act (GADPTRA) of 1988, an Abbreviated New Animal Drug Application (ANADA) may be submitted for a generic version of an approved new animal drug (pioneer product). New target animal safety and effectiveness data and human food safety data (other than tissue residue data) are not required for approval of an ANADA.

Ordinarily, the ANADA Sponsor shows the generic product is bioequivalent to the pioneer, which has been shown to be safe and effective. If bioequivalence is demonstrated through a clinical endpoint study, then a tissue residue study to establish the withdrawal time for the generic product should also be conducted. For certain dosage forms, the agency will grant a waiver from the requirement of an *in vivo* bioequivalence study (55 FR 24645, June 18, 1990; Fifth GADPTRA Policy Letter; Bioequivalence Guideline, October 9, 2002).

Based on the formulation characteristics of the generic product, Med-Pharmex, Inc. was granted a waiver from the requirement of an *in vivo* bioequivalence study for the generic product Euthanasia-III (Euthanasia Solution)(pentobarbital sodium and phenytoin sodium). The generic product is administered as a nonsterile injectable solution, contains the same active ingredients in the same concentration and dosage form as the pioneer product, and contains no inactive ingredients that may significantly affect the absorption of the active ingredients. The pioneer product BEUTHANASIA-D (Euthanasia Solution) (pentobarbital sodium and phenytoin sodium), the subject of Schering-Plough Animal Health Corp.'s, NADA 119-807, was approved on April 4, 1981.

3. HUMAN SAFETY:

This drug is intended for use in dogs, which are non-food animals. Because this new animal drug is not intended for use in food-producing animals, data on human safety pertaining to drug residues in food were not required for approval of this ANADA.

Human Warnings are provided on the product label as follows: "HUMAN WARNING Caution should be exercised to avoid contact of the drug with open wounds or accidental self-inflicted injections. Keep out of reach of children. If eye contact, flush eyes with water and seek medical attention. FOR DOGS ONLY."

4. AGENCY CONCLUSIONS:

This ANADA submitted under section 512(b)(2) of the Federal Food, Drug, and Cosmetic Act satisfies the requirements of section 512(n) of the Act and demonstrates that Euthanasia-III Solution (Euthanasia Solution), when used under its proposed conditions of use, is safe and effective for its labeled indications.

5. ATTACHMENTS:

Facsimile generic labeling and currently approved pioneer labeling are attached as follows:

Generic Labeling for ANADA 200-280:
Euthanasia-III Solution
- 100 mL bottle label (will also be attached to white individual bottle carton)
- Package Insert

Pioneer Labeling for NADA 119-807:
BEUTHANASIA-D Special (Euthanasia Solution)
- 100 mL bottle label
- Package insert
- Individual carton label

cc: Courtesy copy for sponsor
HFV-199, ANADA 200-280 E-0004, T-0005, Orig.
HFV-1, Special Mailing List
HFV-12, FOI Staff
HFV-104, Green Book
HFV-107, Reserve Copy
HFV-120, Labeling Project
HFV-216, Surveillance Copy
✓HFV-230, Compliance Copy
HFA-305, Division of Dockets Management

AWeiss/slr, HFV-104, 11/8/2004

ec: CVM Records\ONADE\\A200280\E0004foi.sum

Warning: For canine euthanasia only
Must not be used for therapeutic purposes.
Do not use in animals intended for food.

Human Warning: Refer to package insert for important human risk information.

Store between 15° and 30°C (59° and 86°F).

ENVIRONMENTAL HAZARD: This product is toxic to wildlife. Birds and mammals feeding on treated animals may be killed. Euthanized animals must be properly disposed of by deep burial, incineration, or other method in compliance with state and local laws, to prevent consumption of carcass material by scavenging wildlife.

C III

100 mL

EUTHANASIA-III SOLUTION

(Euthanasia Solution)

FOR DOGS ONLY

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

MED-PHARMEX, INC.
Pomona, CA 91767

ANADA 200-280.
Approved by FDA.

Manufactured by a non-sterilizing process.
Multiple Dose Vial.

Each mL contains: *active ingredients:* 390 mg pentobarbital sodium (barbituric acid derivative), 50 mg phenytoin sodium. *Inactive ingredients:* 10% ethyl alcohol, 18% propylene glycol, 0.003688 mg rhodamine B, 2% benzyl alcohol (preservative), purified water q.s. Sodium hydroxide and /or hydrochloric acid may be added to adjust pH.

For Intravenous or Intracardiac Use.

Read product information sheet carefully.

See warnings on left panel.

Lot No /
Exp. Date

Warning: For canine euthanasia only
Must not be used for therapeutic purposes.
Do not use in animals intended for food.

Human Warning: Refer to package insert for important human risk information.

Store between 15° and 30°C (59° and 86°F).

ENVIRONMENTAL HAZARD: This product is toxic to wildlife. Birds and mammals feeding on treated animals may be killed. Euthanized animals must be properly disposed of by deep burial, incineration, or other method in compliance with state and local laws, to prevent consumption of carcass material by scavenging wildlife.

C III

100 mL

EUTHANASIA-III SOLUTION

(Euthanasia Solution)

FOR DOGS ONLY

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

MED-PHARMEX, INC.
Pomona, CA 91767

ANADA 200-280
Approved by FDA.

Manufactured by a non-sterilizing process.
Multiple Dose Vial.

Each mL contains: *active ingredients:* 390 mg pentobarbital sodium (barbituric acid derivative), 50 mg phenytoin sodium. *Inactive ingredients:* 10% ethyl alcohol, 18% propylene glycol, 0.003688 mg rhodamine B, 2% benzyl alcohol (preservative), purified water q.s. Sodium hydroxide and /or hydrochloric acid may be added to adjust pH.

For Intravenous or Intracardiac Use.

Read product information sheet carefully.

See warnings on left panel.

Lot No./
Exp. Date

Warning: For canine euthanasia only
Must not be used for therapeutic purposes.
Do not use in animals intended for food.

Human Warning: Refer to package insert for important human risk information.

Store between 15° and 30°C (59° and 86°F).

ENVIRONMENTAL HAZARD: This product is toxic to wildlife. Birds and mammals feeding on treated animals may be killed. Euthanized animals must be properly disposed of by deep burial, incineration, or other method in compliance with state and local laws, to prevent consumption of carcass material by scavenging wildlife.

C III

100 mL

EUTHANASIA-III SOLUTION

(Euthanasia Solution)

FOR DOGS ONLY

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

MED-PHARMEX, INC.
Pomona, CA 91767

ANADA 200-280.
Approved by FDA.

Manufactured by a non-sterilizing process.
Multiple Dose Vial.

Each mL contains: *active ingredients:* 390 mg pentobarbital sodium (barbituric acid derivative), 50 mg phenytoin sodium. *Inactive ingredients:* 10% ethyl alcohol, 18% propylene glycol, 0.003688 mg rhodamine B, 2% benzyl alcohol (preservative), purified water q.s. Sodium hydroxide and /or hydrochloric acid may be added to adjust pH.

For Intravenous or Intracardiac Use.

Read product information sheet carefully.

See warnings on left panel.

Lot No /
Exp. Date

ANADA 200-280

EUTHANASIA-III SOLUTION

(EUTHANASIA SOLUTION)

FOR DOGS ONLY

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION:

A non-sterile solution containing pentobarbital sodium and phenytoin sodium as the active ingredients. Rhodamine B, a bluish-red fluorescent dye, is included in the formulation to help distinguish it from parenteral drugs intended for therapeutic use. Although the solution is not sterile, benzyl alcohol, a bacteriostat, is included to retard the growth of microorganisms.

Each mL contains: *Active ingredients:* 390 mg pentobarbital sodium (barbituric acid derivative), 50 mg phenytoin sodium, *Inactive ingredients:* 10% ethyl alcohol, 18% propylene glycol, 0.003688 mg rhodamine B, 2% benzyl alcohol (preservative), purified water q.s. Sodium hydroxide and/or hydrochloric acid may be added to adjust pH.

ACTIONS:

EUTHANASIA-III SOLUTION contains two active ingredients which are chemically compatible but pharmacologically different. Each ingredient acts in such a manner so as to cause humane, painless and rapid euthanasia. Euthanasia is due to cerebral death in conjunction with respiratory arrest and circulatory collapse. Cerebral death occurs prior to cessation of cardiac activity.

When administered intravenously, pentobarbital sodium produces rapid anesthetic action. There is a smooth and rapid onset of unconsciousness. At the lethal dose, there is depression of vital medullary respiratory and vasomotor centers.

When administered intravenously, phenytoin sodium produces toxic signs of cardiovascular collapse and/or central nervous system depression. Hypotension occurs when the drug is administered rapidly.

PHARMACODYNAMIC ACTIVITY:

The sequence of events leading to humane, painless and rapid euthanasia following intravenous injection of EUTHANASIA-III solution is similar to that following intravenous injection of pentobarbital sodium or other barbituric derivatives. Within seconds, unconsciousness is induced with simultaneous collapse of the dog. This stage rapidly progresses to deep anesthesia with concomitant reduction in the blood pressure. A few seconds later, breathing stops, due to depression of the medullary respiratory center; encephalographic activity becomes isoelectric, indicating cerebral death; and then cardiac activity ceases.

Phenytoin sodium exerts its effect during the deep anesthesia stage caused by the pentobarbital sodium. This ingredient, due to its cardiotoxic properties, hastens the stoppage of electrical activity in the heart.

INDICATIONS:

For use in dogs for humane, painless and rapid euthanasia.

WARNING:

For canine euthanasia only. Must not be used for therapeutic purposes. Do not use in animals intended for food

ENVIRONMENTAL HAZARD:

This product is toxic to wildlife. Birds and mammals feeding on treated animals may be killed. Euthanized animals must be properly disposed of by deep burial, incineration, or other method in compliance with state and local laws, to prevent consumption of carcass material by scavenging wildlife.

HUMAN WARNING:

Caution should be exercised to avoid contact of the drug with open wounds or accidental self-inflicted injections. Keep out of reach of children. If eye contact, flush eyes with water and seek medical attention.

PRECAUTIONS:

Euthanasia may sometimes be delayed in dogs with severe cardiac or circulatory deficiencies. This may be explained by the impaired movement of the drug to its site of action. An occasional dog may elicit reflex responses manifested by motor movement; however, an unconscious animal does not experience pain, because the cerebral cortex is not functioning.

When restraint may cause the dog pain, injury or anxiety, or danger to the person making the injection, prior use of tranquilizing or immobilizing drugs may be necessary.

DOSAGE AND ADMINISTRATION:

Dosage: Dogs: 1 mL for each 10 pounds of body weight

Administration: Intravenous injection is preferred. Intracardiac injection may be made when intravenous injection is impractical, as in a very small dog, or in a comatose dog with impaired vascular functions. Good injection skill is necessary for intracardiac injection.

The calculated dose should be given in a single bolus injection.

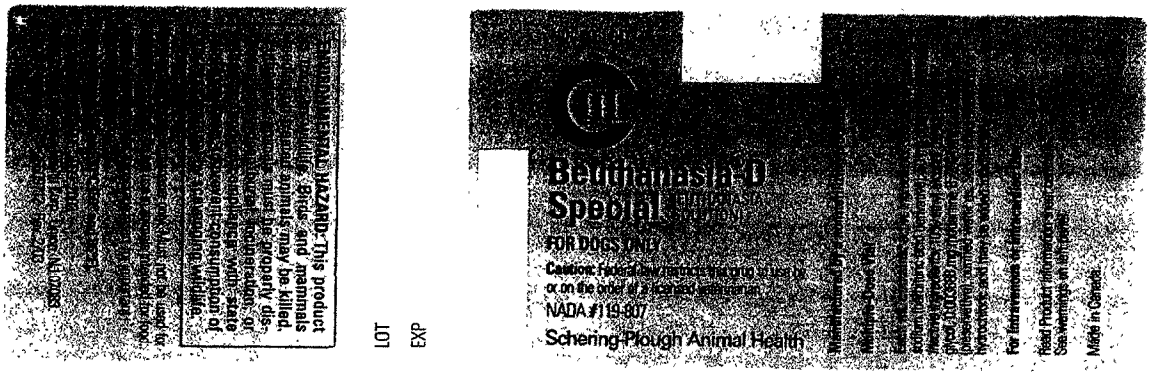
For intravenous injection, a needle of sufficient gauge to ensure intravenous placement of the entire dose should be used. The use of a Luer-Lok® syringe is recommended to prevent accidental exposure to needle/syringe separation.

HOW SUPPLIED: Euthanasia-III Solution is available in 100-mL multiple-dose vials.

Manufactured by a non-sterilizing process.

STORAGE: Store between 15° and 30°C (59°F and 86°F).

Med-Pharmex, Inc.
Pomona, CA 91767
October 2004.



F-26609518

PRODUCT INFORMATION

NADA #119-807

BEUTHANASIA®-D SPECIAL

(EUTHANASIA SOLUTION)

FOR DOGS ONLY

CAUTION Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION A nonsterile solution containing pentobarbital sodium and phenytoin sodium as the active ingredients. Rhodamine B, a bluish-red fluorescent dye, is included in the formulation to help distinguish it from parenteral drugs intended for therapeutic use. Although the solution is not sterile, benzyl alcohol, a bacteriostat, is included to retard the growth of microorganisms.

Each mL contains: *active ingredients:* 390 mg pentobarbital sodium (barbituric acid derivative), 50 mg phenytoin sodium; *inactive ingredients:* 10% ethyl alcohol, 18% propylene glycol, 0.003688 mg rhodamine B, 2% benzyl alcohol (preservative), purified water qs. Sodium hydroxide and/or hydrochloric acid may be added to adjust pH.

ACTIONS BEUTHANASIA-D SPECIAL EUTHANASIA SOLUTION contains two active ingredients which are chemically compatible but pharmacologically different. Each ingredient acts in such a manner so as to cause humane, painless, and rapid euthanasia. Euthanasia is due to cerebral death in conjunction with respiratory arrest and circulatory collapse. Cerebral death occurs prior to cessation of cardiac activity.

When administered intravenously, pentobarbital sodium produces rapid anesthetic action. There is a smooth and rapid onset of unconsciousness. At the lethal dose, there is depression of vital medullary respiratory and vasomotor centers.

When administered intravenously, phenytoin sodium produces toxic signs of cardiovascular collapse and/or central nervous system depression. Hypotension occurs when the drug is administered rapidly.

Pharmacodynamic Activity: The sequence of events leading to humane, painless, and rapid euthanasia following intravenous injection of BEUTHANASIA-D SPECIAL EUTHANASIA SOLUTION is similar to that following intravenous injection of pentobarbital sodium or other barbituric acid derivatives. Within seconds, unconsciousness is induced with simultaneous collapse of the dog. This stage rapidly progresses to deep anesthesia with concomitant reduction in the blood pressure. A few seconds later, breathing stops, due to depression of the medullary respiratory center; encephalographic activity becomes isoelectric, indicating cerebral death, and then cardiac activity ceases.

Phenytoin sodium exerts its effect during the deep anesthesia stage caused by the pentobarbital sodium. This ingredient, due to its cardiotoxic properties, hastens the stoppage of electrical activity in the heart.

(Continued on reverse side)

00

BEUTHANASIA®-D SPECIAL

(EUTHANASIA SOLUTION)

INDICATIONS For use in dogs for humane, painless, and rapid euthanasia.

WARNING For canine euthanasia only. Must not be used for therapeutic purposes. Do not use in animals intended for food.

ENVIRONMENTAL HAZARD: This product is toxic to wildlife. Birds and mammals feeding on treated animals may be killed. Euthanized animals must be properly disposed of by deep burial, incineration, or other method in compliance with state and local laws, to prevent consumption of carcass material by scavenging wildlife.

HUMAN WARNING Caution should be exercised to avoid contact of the drug with open wounds or accidental self-inflicted injections. Keep out of reach of children. If eye contact, flush eyes with water and seek medical attention.

PRECAUTIONS Euthanasia may sometimes be delayed in dogs with severe cardiac or circulatory deficiencies. This may be explained by the impaired movement of the drug to its site of action. An occasional dog may elicit reflex responses manifested by motor movement; however, an unconscious animal does not experience pain, because the cerebral cortex is not functioning.

When restraint may cause the dog pain, injury, or anxiety, or danger to the person making the injection, prior use of tranquilizing or immobilizing drugs may be necessary.

DOSAGE AND ADMINISTRATION

Dosage: Dogs, 1 mL for each 10 pounds of body weight.

Administration: Intravenous injection is preferred. Intracardiac injection may be made when intravenous injection is impractical, as in a very small dog or in a comatose dog with impaired vascular functions. Good injection skill is necessary for intracardiac injection.

The calculated dose should be given in a single bolus injection.

For intravenous injection, a needle of sufficient gauge to ensure intravenous placement of the entire dose should be used. The use of a Luer-Lok® syringe is recommended to prevent accidental exposure due to needle/syringe separation.

HOW SUPPLIED BEUTHANASIA-D SPECIAL EUTHANASIA SOLUTION is available in 100-mL multiple-dose vials, NDC 0061-0473-05.

Manufactured by a nonsterilizing process.

STORAGE Store between 15° and 30°C (59° and 86°F).

Made in Canada.
Schering-Plough Animal Health Corp., Union, NJ 07083

81-482046 Rev. 2/03 B-26609518

LOT
EXP

(EUTHANASIA SOLUTION)

Beuthanasia-D
Special

100 mL

Human Warning: Caution should be exercised to avoid contact of the drug with open wounds or accidental self inflicted injections. Keep out of reach of children. If eye contact, flush eyes with water and seek medical attention.

Warning: For canine euthanasia only. Must not be used for therapeutic purposes. Do not use in animals intended for food.

Store between 15° and 30°C (59° and 86°F).

 26609810 Rev. 2/03

ENVIRONMENTAL HAZARD: This product is toxic to wildlife. Birds and mammals feeding on treated animals may be killed. Euthanized animals must be properly disposed of by deep burial, incineration, or other method in compliance with state and local laws, to prevent consumption of carcass material by scavenging wildlife.

N
3 0061-0473-05 9

NDC 0061-0473-05

Beuthanasia®-D Special

(EUTHANASIA SOLUTION)

FOR DOGS ONLY

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

NADA #119-807

Schering-Plough Animal Health

Manufactured by a nonsterilizing process.

Multiple-Dose Vial

Each mL contains: *active ingredients:* 390 mg pentobarbital sodium (barbituric acid derivative), 50 mg phenytoin sodium. *Inactive ingredients:* 10% ethyl alcohol, 18% propylene glycol, 0.003688 mg rhodamine B, 2% benzyl alcohol (preservative), purified water qs. Sodium hydroxide and/or hydrochloric acid may be added to adjust pH.

For Intravenous or Intracardiac Use.

Read Product Information sheet carefully. See warnings on back panel.

Made in Canada.

N 119-807 L0190 FPL 11/17/2003